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☐ 1: NP\_066961. Reports TNF receptor-asso...[gi:22027612]

BLink, Conserved Domains, Links

LOCUS NP\_066961 501 aa linear PRI 27-NOV-2005

DEFINITION TNF receptor-associated factor 2 [Homo sapiens].

ACCESSION NP\_066961 NP\_663770

VERSION NP\_066961.2 GI:22027612

DBSOURCE REFSEQ: accession NM\_021138.3

KEYWORDS

SOURCE Homo sapiens (human)

ORGANISM Homo sapiens

Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Primates; Catarrhini; Hominidae; Homo.

REFERENCE 1 (residues 1 to 501)

AUTHORS Yang, C.H., Murti, A. and Pfeffer, L.M.

TITLE Interferon induces NF-kappa B-inducing kinase/tumor necrosis factor receptor-associated factor-dependent NF-kappa B activation to promote cell survival

JOURNAL J. Biol. Chem. 280 (36), 31530-31536 (2005)

PUBMED 16009713

REMARK GeneRIF: Results for the first time place tumor necrosis factor receptor-associated factor-2 (TRAF2), previously shown to function in TNF signaling, within the interferon signal transduction pathway

REFERENCE 2 (residues 1 to 501)

AUTHORS Esparza, E.M. and Arch, R.H.

TITLE Glucocorticoid-induced TNF receptor, a costimulatory receptor on naive and activated T cells, uses TNF receptor-associated factor 2 in a novel fashion as an inhibitor of NF-kappa B activation

JOURNAL J. Immunol. 174 (12), 7875-7882 (2005)

PUBMED 15944293

REMARK GeneRIF: In contrast with its effects on signaling triggered by other TNF receptors, functional studies reveal that TRAF2 plays a novel inhibitory role in glucocorticoid-induced TNF receptor (GITR)-triggered NF-kappa B activation.

REFERENCE 3 (residues 1 to 501)

AUTHORS Kim, W.J., Back, S.H., Kim, V., Ryu, I. and Jang, S.K.

TITLE Sequestration of TRAF2 into stress granules interrupts tumor necrosis factor signaling under stress conditions

JOURNAL Mol. Cell. Biol. 25 (6), 2450-2462 (2005)

PUBMED 15743837

REMARK GeneRIF: TRAF2 colocalizes with eIF4GI in insoluble stress granules during cellular exposure to stress conditions.

REFERENCE 4 (residues 1 to 501)

AUTHORS Hauer, J., Puschner, S., Ramakrishnan, P., Simon, U., Bongers, M., Federle, C. and Engelmann, H.

TITLE TNF receptor (TNFR)-associated factor (TRAF) 3 serves as an inhibitor of TRAF2/5-mediated activation of the noncanonical NF-kappaB pathway by TRAF-binding TNFRs

JOURNAL Proc. Natl. Acad. Sci. U.S.A. 102 (8), 2874-2879 (2005)

PUBMED 15708970

REMARK GeneRIF: TRAF3 specifically blocked the NF-kappaB activation via TRAF2/5.

REFERENCE 5 (residues 1 to 501)

AUTHORS He, L., Grammer, A.C., Wu, X. and Lipsky, P.E.

TITLE TRAF3 forms heterotrimers with TRAF2 and modulates its ability to mediate NF-kappaB activation

JOURNAL J. Biol. Chem. 279 (53), 55855-55865 (2004)

PUBMED 15383523

REMARK GeneRIF: there is a novel association between TRAF2 and TRAF3 that is mediated by unique portions of each protein and that specifically regulates activation of NF-kappaB, but not AP-1

REFERENCE 6 (residues 1 to 501)

AUTHORS Zhang, H., Zhang, R., Luo, Y., D'Alessio, A., Pober, J.S. and Min, W.

TITLE AIP1/DAB2IP, a novel member of the Ras-GAP family, transduces TRAF2-induced ASK1-JNK activation

JOURNAL J. Biol. Chem. 279 (43), 44955-44965 (2004)

PUBMED 15310755

REMARK GeneRIF: AIP1 is a novel transducer in TNF-induced TRAF2-dependent activation of ASK1 that mediates a balance between JNK versus

NF-kappaB signaling  
7 (residues 1 to 501)  
REFERENCE  
AUTHORS Vischioni,B., Giaccone,G., Span,S.W., Kruyt,F.A. and Rodriguez,J.A.  
TITLE Nuclear shuttling and TRAF2-mediated retention in the cytoplasm  
regulate the subcellular localization of cIAP1 and cIAP2  
JOURNAL Exp. Cell Res. 298 (2), 535-548 (2004)  
PUBMED 15265700  
REMARK GeneRIF: TRAF2 plays an important role as regulator of IAP  
nucleocytoplasmic localization, by preventing nuclear translocation  
of cIAP1 and cIAP2.

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REFERENCE  
AUTHORS Fotin-Mieczek,M., Henkler,F., Hausser,A., Glauner,H., Samel,D.,  
Graness,A., Scheurich,P., Mauri,D. and Wajant,H.  
TITLE Tumor necrosis factor receptor-associated factor (TRAF) 1 regulates  
CD40-induced TRAF2-mediated NF-kappaB activation  
JOURNAL J. Biol. Chem. 279 (1), 677-685 (2004)  
PUBMED 14557256  
REMARK GeneRIF: stoichiometry of TRAF1-TRAF2 heteromeric complexes  
((TRAF2)2-TRAF1 versus TRAF2-(TRAF1)2) determines their capability  
to mediate CD40 signaling but has no major effect on TNF signaling

9 (residues 1 to 501)  
REFERENCE  
AUTHORS Sakurai,H., Suzuki,S., Kawasaki,N., Nakano,H., Okazaki,T.,  
Chino,A., Doi,T. and Saiki,I.  
TITLE Tumor necrosis factor-alpha-induced IKK phosphorylation of  
NF-kappaB p65 on serine 536 is mediated through the TRAF2, TRAF5,  
and TAK1 signaling pathway  
JOURNAL J. Biol. Chem. 278 (38), 36916-36923 (2003)  
PUBMED 12842894  
REMARK GeneRIF: TRAF2 has a role in TNF-alpha induced IKK phosphorylation  
of NF-kappaB p65

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REFERENCE  
AUTHORS Kaneko,M., Niinuma,Y. and Nomura,Y.  
TITLE Activation signal of nuclear factor-kappa B in response to  
endoplasmic reticulum stress is transduced via IRE1 and tumor  
necrosis factor receptor-associated factor 2  
JOURNAL Biol. Pharm. Bull. 26 (7), 931-935 (2003)  
PUBMED 12843613

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REFERENCE  
AUTHORS Shi,C.S. and Kehrl,J.H.  
TITLE Tumor necrosis factor (TNF)-induced germinal center kinase-related  
(GCKR) and stress-activated protein kinase (SAPK) activation  
depends upon the E2/E3 complex Ubc13-Uev1A/TNF receptor-associated  
factor 2 (TRAF2)  
JOURNAL J. Biol. Chem. 278 (17), 15429-15434 (2003)  
PUBMED 12591926  
REMARK GeneRIF: TNF signaling leads to oligomerization, ubiquitination,  
and activation of GCKR and activation of the SAPK pathway in a  
manner that depends upon TRAF2 polyubiquitination and  
oligomerization and Ubc13 function

12 (residues 1 to 501)  
REFERENCE  
AUTHORS Kuai,J., Nickbarg,E., Wooters,J., Qiu,Y., Wang,J. and Lin,L.L.  
TITLE Endogenous association of TRAF2, TRAF3, cIAP1, and Smac with  
lymphotoxin beta receptor reveals a novel mechanism of apoptosis  
JOURNAL J. Biol. Chem. 278 (16), 14363-14369 (2003)  
PUBMED 12571250  
REMARK GeneRIF: TRAF2, TRAF3, cIAP1, Smac, and lymphotoxin beta receptor  
associate and are involved in apoptosis

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REFERENCE  
AUTHORS Munzert,G., Kirchner,D., Stobbe,H., Bergmann,L., Schmid,R.M.,  
Dohner,H. and Heimpel,H.  
TITLE Tumor necrosis factor receptor-associated factor 1 gene  
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JOURNAL Blood 100 (10), 3749-3756 (2002)  
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REFERENCE  
AUTHORS Habelhah,H., Frew,I.J., Laine,A., Janes,P.W., Relaix,F.,  
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JOURNAL EMBO J. 21 (21), 5756-5765 (2002)  
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REFERENCE  
AUTHORS Zhou,R., Bonneaud,N., Yuan,C.X., de Santa Barbara,P., Boizet,B.,  
Schomber,T., Scherer,G., Roeder,R.G., Poulat,F. and Berta,P.  
TITLE SOX9 interacts with a component of the human thyroid hormone  
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JOURNAL Nucleic Acids Res. 30 (14), 3245-3252 (2002)  
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REFERENCE  
AUTHORS Brown,K.D., Hostager,B.S. and Bishop,G.A.  
TITLE Regulation of TRAF2 signaling by self-induced degradation  
JOURNAL J. Biol. Chem. 277 (22), 19433-19438 (2002)  
PUBMED 11909853

REFERENCE 17 (sites)  
AUTHORS Brown, K.D., Hostager, B.S. and Bishop, G.A.  
TITLE Regulation of TRAF2 signaling by self-induced degradation  
JOURNAL J Biol Chem 277 (22), 19433-19438 (2002)  
PUBMED 11909853

REFERENCE 18 (residues 1 to 501)  
AUTHORS Eliopoulos, A.G., Davies, C., Blake, S.S., Murray, P., Najafipour, S.,  
Tsichlis, P.N. and Young, L.S.  
TITLE The oncogenic protein kinase Tpl-2/Cot contributes to Epstein-Barr  
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signaling downstream of TRAF2  
JOURNAL J. Virol. 76 (9), 4567-4579 (2002)  
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REFERENCE 19 (residues 1 to 501)  
AUTHORS Hostager, B.S. and Bishop, G.A.  
TITLE Role of TNF receptor-associated factor 2 in the activation of IgM  
secretion by CD40 and CD120b  
JOURNAL J. Immunol. 168 (7), 3318-3322 (2002)  
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REFERENCE 20 (residues 1 to 501)  
AUTHORS Li, X., Yang, Y. and Ashwell, J.D.  
TITLE TNF-RII and c-IAP1 mediate ubiquitination and degradation of TRAF2  
JOURNAL Nature 416 (6878), 345-347 (2002)  
PUBMED 11907583  
REMARK GenerIF: TNF-RII and c-IAP1 mediate its ubiquitination

REFERENCE 21 (sites)  
AUTHORS Li, X., Yang, Y. and Ashwell, J.D.  
TITLE TNF-RII and c-IAP1 mediate ubiquitination and degradation of TRAF2  
JOURNAL Nature 416 (6878), 345-347 (2002)  
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REFERENCE 22 (residues 1 to 501)  
AUTHORS Cao, H., Courchesne, W.E. and Mastick, C.C.  
TITLE A phosphotyrosine-dependent protein interaction screen reveals a  
role for phosphorylation of caveolin-1 on tyrosine 14: recruitment  
of C-terminal Src kinase  
JOURNAL J. Biol. Chem. 277 (11), 8771-8774 (2002)  
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REFERENCE 23 (residues 1 to 501)  
AUTHORS Xia, P., Wang, L., Moretti, P.A., Albanese, N., Chai, F., Pitson, S.M.,  
D'Andrea, R.J., Gamble, J.R. and Vadas, M.A.  
TITLE Sphingosine kinase interacts with TRAF2 and dissects tumor necrosis  
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JOURNAL J. Biol. Chem. 277 (10), 7996-8003 (2002)  
PUBMED 11777919  
REMARK GenerIF: These findings show a role for SphK in the signal  
transduction by TRAF2 specifically leading to activation of  
NF-kappa B and antiapoptosis.

REFERENCE 24 (residues 1 to 501)  
AUTHORS Yan, M., Zhang, Z., Brady, J.R., Schilbach, S., Fairbrother, W.J. and  
Dixit, V.M.  
TITLE Identification of a novel death domain-containing adaptor molecule  
for ectodysplasin-A receptor that is mutated in crinkled mice  
JOURNAL Curr. Biol. 12 (5), 409-413 (2002)  
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REFERENCE 25 (residues 1 to 501)  
AUTHORS Kanamori, M., Suzuki, H., Saito, R., Muramatsu, M. and Hayashizaki, Y.  
TITLE T2BP, a novel TRAF2 binding protein, can activate NF-kappaB and  
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JOURNAL Biochem. Biophys. Res. Commun. 290 (3), 1108-1113 (2002)  
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REFERENCE 26 (residues 1 to 501)  
AUTHORS Oukka, M., Kim, S.T., Lugo, G., Sun, J., Wu, L.C. and Glimcher, L.H.  
TITLE A mammalian homolog of Drosophila schnurri, KRC, regulates TNF  
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AUTHORS Wiley, S.R., Cassiano, L., Lofton, T., Davis-Smith, T., Winkles, J.A.,  
Lindner, V., Liu, H., Daniel, T.O., Smith, C.A. and Fanslow, W.C.  
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REFERENCE 28 (residues 1 to 501)  
AUTHORS Choi, Y.H., Kim, K.B., Kim, H.H., Hong, G.S., Kwon, Y.K., Chung, C.W.,  
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TITLE FLASH coordinates NF-kappa B activity via TRAF2  
JOURNAL J. Biol. Chem. 276 (27), 25073-25077 (2001)  
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AUTHORS Lieberman, R., Mowen, K.A., McBride, K.D., Leautaud, V., Zhang, X.,  
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the T helper cell type 2 response through interaction with NFAT-interacting protein (NIP45)

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 AUTHORS Eby, M.T., Jasmin, A., Kumar, A., Sharma, K. and Chaudhary, P.M.  
 TITLE TAJ, a novel member of the tumor necrosis factor receptor family, activates the c-Jun N-terminal kinase pathway and mediates caspase-independent cell death  
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 REFERENCE 42 (residues 1 to 501)  
 AUTHORS Yoneda, T., Imaizumi, K., Maeda, M., Yui, D., Manabe, T., Katayama, T., Sato, N., Gomi, F., Morihara, T., Mori, Y., Miyoshi, K., Hitomi, J., Ugawa, S., Yamada, S., Okabe, M. and Tohyama, M.  
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 REFERENCE 43 (residues 1 to 501)  
 AUTHORS Urano, F., Wang, X., Bertolotti, A., Zhang, Y., Chung, P., Harding, H.P. and Ron, D.  
 TITLE Coupling of stress in the ER to activation of JNK protein kinases by transmembrane protein kinase IRE1  
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 JOURNAL J. Biol. Chem. 275 (1), 271-278 (2000)  
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 AUTHORS Pomerantz, J.L. and Baltimore, D.  
 TITLE NF-kappaB activation by a signaling complex containing TRAF2, TANK and TBK1, a novel IKK-related kinase  
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 AUTHORS Fu, C.A., Shen, M., Huang, B.C., Lasaga, J., Payan, D.G. and Luo, Y.  
 TITLE TNK1, a novel member of the germinal center kinase family that activates the c-Jun N-terminal kinase pathway and regulates the cytoskeleton  
 JOURNAL J. Biol. Chem. 274 (43), 30729-30737 (1999)  
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 AUTHORS Ye, X., Mehlen, P., Rabizadeh, S., VanArsdale, T., Zhang, H., Shin, H., Wang, J.J., Leo, E., Zapata, J., Hauser, C.A., Reed, J.C. and Bredesen, D.E.  
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 and NFkappaB  
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 Dougall, W.C.  
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 On or before Feb 13, 2004 this sequence version replaced  
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Summary: The protein encoded by this gene is a member of the TNF  
 receptor associated factor (TRAF) protein family. TRAF proteins  
 associate with, and mediate the signal transduction from members of  
 the TNF receptor superfamily. This protein directly interacts with  
 TNF receptors, and forms a heterodimeric complex with TRAF1. This  
 protein is required for TNF-alpha-mediated activation of MAPK8/JNK  
 and NF-kappaB. The protein complex formed by this protein and TRAF1  
 interacts with the inhibitor-of-apoptosis proteins (IAPs), and  
 functions as a mediator of the anti-apoptotic signals from TNF  
 receptors. The interaction of this protein with TRADD, a TNF  
 receptor associated apoptotic signal transducer, ensures the  
 recruitment of IAPs for the direct inhibition of caspase  
 activation. BIRC2/c-IAP1, an apoptosis inhibitor possessing  
 ubiquitin ligase activity, can ubiquitinate and induce the  
 degradation of this protein, and thus potentiate TNF-induced  
 apoptosis. Multiple alternatively spliced transcript variants have  
 been found for this gene, but the biological validity of only one  
 transcript has been determined.

FEATURES Location/Qualifiers



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